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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,625	11/02/2006	Stephen J. Klaus	FP0617 US	7369

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409 Illinois Street
San Francisco, CA 94158

EXAMINER	
OGUNBIYI, OLUWATOSIN A	

ART UNIT	PAPER NUMBER
1645	

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06/10/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,625	KLAUS ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,12-16,27-33,36,48 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 12-16, 27-33, 36 and 48-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 3/26/10 has been entered into the record. Claims 2-11, 17-26, 34-35 and 37-47 are cancelled. Claims 1, 12-13, 16, 27-31 and 36 are amended. Claims 1, 12-16, 27-33, 36 and 48-49 are pending and are under examination.

Rejections Withdrawn

2. The rejection of claim 16 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 16 of copending Application No. 11/348,294 is withdrawn in view of the abandonment of the 11/348,294 application.

3. The rejection of claims 1, 9-16, 19 and 21-27 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9, 10, 11-16, 17-24, 34-56 of copending Application No.11/348294 ('294) is withdrawn in view of the abandonment of the 11/348,294 application.

4. The rejection of claims 1, 9-16, 19, 21-27, 28-33 and 36 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9, 10, 11-16, 17-24, 34-56 of copending Application No.11/348294 ('294) in view of Bohmer et al WO 01/12784 A1 22 February 2001 is withdrawn in view of the abandonment of the 11/348,294 application.

5. The rejection of claims 28-33 and 36 rejected under 35 U.S.C. 112, first paragraph (scope of enablement) is withdrawn in view of the amendment to base claim 28 which now recites "population of cells derived from bone marrow".

6. The rejection of claims 25-27 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment to the claim 1 and 27.

7. The rejection of claims 1, 9-16, 19, 21-27 and 48-49 under 35 U.S.C. 102(e) as being anticipated by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293, cited previously and as evidenced by Perrine et al (Blood, W.B. Saunders, Philadelphia, PA. U.S., 7/1/89, col. 74, No.1, p.454-459, cited in IDS) and as evidenced by Ley et al (Annu Rev Med, 1985, Vol. 36, pp.485-498, cited in IDS) is withdrawn in view of the amendment to the claims and in favor of a new rejection based on the amendment to the claims.

8. The rejection of claims 1, 9-16, 19, 21-27, 28-33, 36 and 48-49 are rejected under 35 U.S.C. 103(a) as being obvious over Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 as evidenced by Pace et al. Experimental

Hematology 2000, 28:283-293, cited previously and as evidenced by Perrine et al. Blood, W.B. Saunders, Philadelphia, PA. U.S., 7/1/89, col. 74, No.1, p.454-459, cited in IDS and as evidenced by Ley et al. Annu Rev Med, 1985, Vol. 36, pp.485-498, cited in IDS) in view of Bohmer et al WO 01/12784 A1 22 February 2001, cited previously is withdrawn in view of the amendment to the claims and in favor of a new rejection based on the amendment to the claims.

New Rejections Based on Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 12-16, and 48-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a subject having hemoglobinopathy, the method comprising administering to the subject in need thereof a compound, wherein the compound inhibits hypoxia inducible factor (HIF) prolyl hydroxylase and wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell, or hematopoietic stem cells or blast forming unit erythroid (BFU-E) cells in the subject; does not reasonably provide enablement for a method for treating a subject having hemoglobinopathy , the method comprising administering to the subject in need thereof a compound, wherein the compound inhibits hypoxia inducible factor (HIF) prolyl hydroxylase and wherein the compound increases expression of the gene encoding γ-globin in other population of cells. **This is a scope of enablement rejection.**

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, the amount of direction provided by the inventor, the existence of working examples, state of the prior art, the level of predictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention and Breadth of the Claims

The claims are drawn to a method for treating a subject having hemoglobinopathy, the method comprising administering to the subject in need thereof a compound, wherein the compound inhibits hypoxia inducible factor (HIF) prolyl hydroxylase and wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell or population of cells.

The scope of the claims requires that the compound that inhibits (HIF) prolyl hydroxylase increase expression of the gene encoding γ-globin in any type of cell population which includes any type of organism derived cell including skin cells, brain cells, neurons, T cells, B cells bone marrow cells, BFU-E cells, hematopoietic stem cells etc and also that the proportion of fetal hemoglobin relative to non-fetal hemoglobin is increased in any population of cells in a subject.

The presence or absence of working examples and guidance in the specification

The specification discloses increased gamma globin expression and induction of fetal hemoglobin in erythroid cell line K562 using a hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor (example 4 from p. 24) and induction of fetal hemoglobin in bone marrow cell cultures. The specification contemplates increasing endogenous gamma globin in hematopoietic stem cells, BFU-E cells and bone marrow cells p. 5 paragraph 16.

The State of the Prior Art and the level of predictability in the art

The art teaches that expression of the gene encoding gamma globin normally occurs in erythroid progenitor cells such as BFU-E cells as evidenced by Perrine et al, see title and abstract, p. 454 under materials and methods, p. 457 column 2 second to last paragraph (cited in IDS) and or hematopoietic/erythroid bone marrow stem cells which retain the capability to produce fetal hemoglobin which comprises gamma globin (see Ley et al p. 488 under "regulation and modulation of HBF synthesis in red blood cell precursors". Thus, only erythroid progenitor cells such as BFU-E cells, hematopoietic stem cells and bone marrow derived cells have the inherent capability of gamma globin gene expression and thus fetal hemoglobin expression.

The art at the time of the instant invention does not teach that other organism derived cells that are not erythroid progenitor cells have this capability of gamma globin gene expression and thus fetal hemoglobin production. The specification also does not provide any evidence for such and does not specifically teach gamma globin gene expression in other types of cells such as brain cells or skin cells or T cells or B cells, to name a few.

Therefore, these other types of organism derived cells are not capable of gamma globin gene expression, will mostly likely not lead to increased gamma gene expression and an increase in the level of fetal hemoglobin in a subject as claimed absent other evidence to the contrary.

See, e.g., *Chiron Corp. v. Genentech Inc.,* 363F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a specific and useful teaching.' The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge

independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology." (citations omitted)).< The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In the instant case, without further guidance, it one skilled in the art cannot readily anticipate the increase in gamma globin gene expression in cells other than those programmed to express gamma globin.

Therefore, undue experimentation would be required of the skilled artisan to practice the full scope of the instant invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1, 12-13, 15-16, 27 and 48-49 are rejected under 35 U.S.C. 102(e) as being anticipated by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to a method for treating a subject having hemoglobinopathy, the method comprising administering to the subject in need thereof a compound, wherein the compound inhibits hypoxia inducible factor (HIF) prolyl hydroxylase and wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell or population of cells.

Klaus et al discloses a method for treating a subject having anemia related conditions or disorders such as hemoglobinopathy such as abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80) comprising administering to a subject in need thereof a compound which inhibits HIF prolyl hydroxylase (see p. 2 paragraph 17-18) wherein the compound is an hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14). Said 2 oxoglutarate mimetic inhibits (HIF) prolyl hydroxylase competitively with respect to 2 oxoglutarate and non-competitively with respect to iron (see paragraph 110).

The hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14) inherently have the property of increasing expression of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cells in the subject and thus increasing the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by bone marrow derived cells in said subject.

Although, Klaus et al does not specifically disclose the inherent functioning of said compounds that inhibits (HIF) prolyl hydroxylase i.e. increasing expressing of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cells in the subject, "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." Id.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 12-16, 27 and 48-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 in view of Perrine et al. WO 93/18761, 1993, cited in IDS.

The claims are drawn to a method for treating a subject having hemoglobinopathy, the method comprising administering to the subject in need thereof a compound, wherein the compound inhibits hypoxia inducible factor (HIF) prolyl hydroxylase and wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell or population of cells.

Klaus et al discloses a method for treating a subject having anemia related conditions or disorders such as hemoglobinopathy such as abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80) comprising administering to a subject in need thereof a compound which inhibits HIF prolyl hydroxylase (see p. 2 paragraph 17-18) wherein the compound is an hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14). Said 2 oxoglutarate mimetic inhibits (HIF) prolyl hydroxylase competitively with respect to 2 oxoglutarate and non-competitively with respect to iron (see paragraph 110).

The hydroxamate[2] (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14) inherently have the property of increasing expression of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cells in the subject and thus increasing the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by bone marrow derived cells in said subject.

Although, Klaus et al does not specifically disclose the inherent functioning of said compounds that inhibits (HIF) prolyl hydroxylase i.e. increasing expressing of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cells in the subject, "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." Id.

Klaus et al does not teach that the hemoglobinopathy is β^{o}- or β^{+}- β thalassemia.

Perrine et al teach other types of β thalassemia such as β^{o}- or β^{+}-. See p. 2 lines 16-30.

It would have been prima facie obvious to one of ordinary skill in the art to have used the method of Klaus et al to treat other β thalassemia disorders such as β^{o}- or β^{+}-, thus resulting in the instant invention with a reasonable expectation of success. The motivation to do so is that Klaus et al teach that hemoglobinopathy such as abnormal hemoglobin such as beta thalassemia can be treated by administering HIF prolyl hydroxylase inhibitors such as hydroxamate or structural mimetics of 2 oxo-glutarate.

12. Claims 28-31, 33 and 36 are rejected under 35 U.S.C. 103(a) as being obvious over Bohmer et al WO 01/12784 A1 22 February 2001, cited previously in view of Skarpidi et al. Experimental Hematology 31 (March 2003) 197-203 as evidenced by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002.

The claims are drawn to a method for increasing the level of fetal hemoglobin levels in a subject, the method comprising administering ex vivo to a population of cells derived from bone marrow a hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma –globin and transfusing the gamma globin expressing cells into the subject.

Bohmer et al teach a method for increasing the level of fetal hemoglobin in a subject having hemoglobinopathy such as beta thalassemia (partial or complete defect in expression of the β-globin gene) and sickle cell syndrome such as sickle cell trait and

sickle cell anemia comprising *administering ex vivo* to a population of bone marrow derived cells (such as hematopoietic stem cells) an agent which increase the number of fetal hemoglobin producing cells (resulting from increased expression of the gene encoding gamma globin) and transferring said cells into the subject (column 2 lines 10-25, column 5 and column 6 under detailed description of the invention and column 12 claims 1-5).

Bohmer et al does not teach that the agent is a hypoxia inducible factor prolyl hydroxylase inhibitor which increases expression of the gene encoding γ-globin.

Skarpidi et al teach hydroxamate (which have the inherent biochemical property of also being inhibitor of hypoxia inducible factor prolyl hydroxylase [1]) iron chelators which increase the level of fetal hemoglobin as wells increase the expression of the gene encoding γ-globin and Skarpidi et al teach that said hydroxamate iron chelators are potent inducers of γ-globin gene expression. See abstract. Skarpidi et al suggest that these hydroxamate iron chelators for treatment of beta thalassemia and sickle cell disease (see p. 202 column 1 first incomplete paragraph and last bridging paragraph to column 2).

"[T]he discovery of a previously unappreciated property of a prior art composition [[in the instant case the hydroxamate iron chelator being inhibitor of hypoxia inducible factor prolyl hydroxylase]], or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." Id.

[1]As evidenced by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002, hydroxamates have the inherent biochemical property of also being inhibitor of hypoxia inducible factor prolyl hydroxylase. See p. 31 claim 36.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to have used the hydroxamate iron chelator of Skarpidi et al in the method of Bohmer et al to increase the level of fetal hemoglobin as well as increase the expression of the gene encoding γ-globin, thus resulting in the instant invention with a reasonable expectation of success. The motivation to do so is because Skarpidi et al teach that said hydroxamate iron chelators are potent inducers of γ-globin gene expression and increase fetal hemoglobin and suggests these hydroxamate iron chelators for treatment of beta thalassemia and sickle cell disease.

13. Claim 32 is rejected under 35 U.S.C. 103(a) as being obvious over Bohmer et al WO 01/12784 A1 22 February 2001, cited previously and Skarpidi et al. Experimental Hematology 31 (March 2003) 197-203 and as evidenced by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 as applied to claims 28-31,33 and 36 above, further in view of Perrine et al. WO 93/18761, 1993, cited in IDS.

The combination of Bohmer et al and Skarpidi et al as evidenced by Klaus et al is set forth supra. Said combination does not teach that the hemoglobinopathy is β^{o} - or β^{+}- β thalassemia.

Perrine et al teach other types of β thalassemia such as β^{o} - or β^{+}- that can be treated by increasing the level of fetal hemoglobin. See p. 2 lines 16-30.

It would have been prima facie obvious to one of ordinary skill in the art to have used the method of the combination of Bohmer et al and Skarpidi et al as evidenced by Klaus et al to treat other β thalassemia disorders such as β^{o} - or β^{+}-, thus resulting in the instant invention with a reasonable expectation of success. The motivation to do so is because Perrine et al teach that β thalassemia such as β^{o} - or β^{+}- can be treated by increasing the level of fetal hemoglobin.

Prior Art Made of Record Pertinent to Applicants Disclosure

[1] Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002, hydroxamates have the inherent biochemical property of also being inhibitor of hypoxia inducible factor prolyl hydroxylase. See p. 31 claim 36.

[2]Skarpidi et al (Experimental Hematology 31 (March 2003) 197-203) teach hydroxamate iron chelators (which have the inherent biochemical property of also being inhibitor of hypoxia inducible factor prolyl hydroxylase) which increase the level of fetal hemoglobin as well as increase the expression of the gene encoding γ-globin and Skarpidi et al teach that said hydroxamate iron chelators are potent inducers of γ-globin gene expression. See abstract. Skarpidi et al suggest that these hydroxamate iron chelators for treatment of beta thalassemia and sickle cell disease (see p. 202 column 1 first incomplete paragraph and last bridging paragraph to column 2).

Status of Claims

Claims 1, 12-16, 27-33, 36 and 48-49 are rejected. No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am- 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645